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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/369,735	08/06/99	MATSUI	I 11059/002001

020985
FISH & RICHARDSON, PC
4350 LA JOLLA VILLAGE DRIVE
SUITE 500
SAN DIEGO CA 92122

HM12/0206

EXAMINER	
MONSHIPOURI, M	
ART UNIT	PAPER NUMBER
1652	12

DATE MAILED: 02/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/369,735	Matsui et al.
Examiner	**Group Art Unit**
Maryam Monshipouri	1652

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-13* is/are pending in the applicat

Of the above, claim(s) *3-11* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 2, 12, and 13* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Claims 1-2 and newly presented claims 12-13 are still at issue and are present for examination. Claims 3-11 are withdrawn as drawn to non-elected invention.

Applicants' arguments filed on 11/27/00 (paper # 11) and his/her declaration with regards to Deposit of Biological Materials (paper #10), have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

The specification is objected to for not complying with sequence rules. Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited in the specification specially those in Brief description of Drawings. See particularly 37 CFR 1.821(d).

Claim Objections

1. Claim 13 is objected to because of the following informalities: this claim depends from itself. Appropriate correction is required. For examination purposes it is assumed that claim 13 depends from claim 12.

2. Claim 12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 12 recites "[t]he enzyme of claim 1..."but its structure is different than said enzyme and thus cannot be dependent from claim 1. **For examining purposes**

it is assumed that claim 12 is an independent claim directed to an enzyme variant with no specific function.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 12-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated thermophilic enzyme having beta-glucosidase activity, wherein up to 2 amino acids of SEQ ID NO:2 are replaced except for amino acids at following positions Q at 19, H at 111, Nat 154, E at 155, Y at 267, E at 324, W at 362, E at 369 and W at 370 while retaining beta-glucosidase activity, does not reasonably provide enablement for enzyme variants with up to 18 or 30 amino acids are simultaneously replaced **with no enzymatic activity at elevated temperatures.** As stated above claims 12 (and its dependent claim 13) is improperly dependent and for examination purposes it is assumed to be directed to beta-glucosidase variants wherein up to 18 or 30 amino acids at any position (including the ones at the active site) may be simultaneously or sequentially replaced except for indicated conserved residues with no specific function. Thus, said claims are directed to a large quantity of enzyme variants most of which are likely to have different function and structure relative to the subject matter of this invention.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2n 1400 (Fed. Cir. 1988) are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

The specification does not teach any variants wherein up to 18 amino acids of said enzyme are replaced while conserving the indicated residues (see claim 12) wherein the enzyme activity and thermal stability is preserved. No examples of claimed enzyme variants with beta-glucosidase activity and thermal stability is provided either. Applicant recited the conserved consensus residues in claim 12, based on the comparison of residues involved in inhibitor binding to polymixa beta-glucosidase (see page 22 of the specification) and merely **speculated** that preservation of corresponding residues in claimed enzyme should result in preserving enzyme activity and thermal stability in variants wherein up to 18 or 30 amino acids may be simultaneously or sequentially replaced with any amino acid residue of any structure, **with no supporting data**. Further, a clear examination of figure 5, indicates that consensus residues at the active site of beta-glucosidase comprise more than those recited in claims 12-13. Current state of prior art indicates that substituting several residues of an active enzyme including consensus residues at the active site (with any amino acid of any structure) apart from claimed conserved residues usually results in disturbing the integrity of enzyme structure and its three dimensional

conformation such that it can no longer fold normally, thereby resulting in **loss of enzyme activity at elevated temperatures**.

Therefore, due to lack of sufficient guidance and relevant examples about the claimed variants in the specification and due to unpredictability of prior art with regards to determining enzyme variant structures with beta-glucosidase activity and thermal stability one of ordinary skill in the art has to go through the burden of undue experimentation in order to prepare thermally stable enzyme variants (i.e. those that are stable at 100 °C or higher) and screen them for enzymatic activity. Thus, the claimed invention goes beyond the scope of the disclosure.

5. Claims 12-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As mentioned above claims 12-13 are confusing and are assumed to be directed to enzyme variants with no specific function.

Claims 12-13 are directed to a genus of modified polypeptide derived from SEQ ID NO:2 , modified by at least one substitution of an amino acid residue in SEQ ID NO:2 with no specific activity at elevated temperatures that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:2 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptide. The specification does not contain any disclosure of the function of all the polypeptide sequences

derived from SEQ ID NO:2 within the scope of the claimed genus. The genus of polypeptide claimed is a large variable genus including peptides which can have a wide variety of functions and with the potentiality of generating many different antibodies. Therefore many functionally unrelated polypeptide are encompassed within the scope of these claims. The specification discloses does not even disclose a single species of the claimed genus to even attempt to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawarabayasi et al. (DNA Research, 5, 55-76, April, 1998) in view of Sambrook et al. (Molecular Cloning, Laboratory Manual, second edition, Cold Spring Harbor Laboratory Press, 1989). Kawarabayasi

teaches the complete sequence and gene organization of the genome of *Pyrococcus horikoshii* OT3 including the sequence comprising an open reading frame (ORF) encoding Beta-glycosidase of the instant invention (i.e. SEQ ID NO:2) prior to foreign priority date of instant invention. In the list of ORF's showing similarities to registered genes (see page 62) with known and unknown function is ORF ID# PH0366 which is predicted to encode beta-glucosidase as claimed instantly. Kawarabayasi does not explicitly teach expression of their ORF# PH0366 gene product.

Sambrook teaches the state of the art techniques in DNA sequence cloning and expression.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to start with the open reading frame # PH 0366 of Kawarabayasi and clone it in an appropriate vector according to Sambrook which could then be transformed in an appropriated host which when grown at appropriate fermentation conditions would result is isolation of large quantities of claimed Beta-glucosidase. One of ordinary skill in the art would be motivated to prepare Beta-glucosidase of Kawarabayasi recombinantly because said polypeptide are useful biocatalysts for synthesizing heterosaccharides at elevated temperatures. In addition, the thermally stable beta-glucosidase is suitable additive for laundry detergents.

Applicant is reminded that although Kwarabayasi does not explicitly teach that their ORF expression product is a tetramer with optimum temperature of 100° C or higher, these properties are inherent to the recombinantly expressed polypeptide, rendering claims 1-2 obvious. One of

ordinary skill in the art would expect that the enzyme is thermally stable because it is isolated from a thermophilic microorganism.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Maryam Monshipouri, Ph.D. whose telephone number is (703) 308-1083. The examiner can normally be reached between 8:00 a.m. and 5:00 p.m. daily except for Fridays.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. P. Achutamurthy, can be reached at (703) 308-3804. The OFFICIAL fax number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Monshipouri

Maryam Monshipouri, Ph.D.

Patent Examiner